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Examiner Yevgeny Valenrod Fax No. (571) 273-9049  
USPTO General Fax No.: (571) 273-8300  
Date of Transmissions: October 26, 2007

Attorney Docket No. 24852-501 CIP

**AMENDMENT****Amendments to the Claims:**

Please amend the claims as follows, without prejudice:

**In the Claims:**

1. (Cancelled)
2. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I characterized by an X-ray diffraction pattern including characteristic peaks at about 9.0, 9.4, 17.5, 19.4, 20.0, 24.0, 24.4, 24.8, 25.0, 28.0, and 43.3 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.
3. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I characterized by an X-ray diffraction pattern including characteristic peaks at about 9.0, 9.4, 17.5, 19.4, 20.0, 24.0, 24.4, 24.8, 25.0, 28.0, 43.3 degrees 2 $\theta$ , and lacking at least one peak at about <8.7, 10.0-10.2, 13.4-14.0, 15.0-15.2, 17.5-19.0, 20.1-20.3, 21.1-21.3, 22.0-22.22, 22.7-23.0, 25.0-25.5, 26.0-26.2, and 27.4-27.6 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.
4. (Cancelled)
5. (Cancelled)
6. (Cancelled)
7. (Cancelled)
8. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I ~~produced-obtainable~~ by a purification process comprising the step of recrystallizing a crude preparation of SAHA from an organic solvent or a mixture of an organic solvent and water, ~~with the proviso that the use of acetonitrile alone is excluded wherein~~

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the organic solvent is at least one of methanol, ethanol or isopropanol, the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at about 9.0, 9.4, 17.5, 19.4, 20.0, 24.0, 24.4, 24.8, 25.0, 28.0, and 43.3 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.

9. (Cancelled)

10. (Cancelled)

11. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I obtainable by a purification process comprising the step of recrystallizing a crude preparation of SAHA from an organic solvent or a mixture of an organic solvent and water, wherein the organic solvent is at least one of methanol, ethanol or isopropanol, the SAHA Form I is ~~The SAHA Form I according to claim 8,~~ further characterized by an X-ray diffraction pattern including characteristic peaks at about 9.0, 9.4, 17.5, 19.4, 20.0, 24.0, 24.4, 24.8, 25.0, 28.0, 43.3 degrees 2 $\theta$ , and lacking at least one peak at about <8.7, 10.0-10.2, 13.4-14.0, 15.0-15.2, 17.5-19.0, 20.1-20.3, 21.1-21.3, 22.0-22.22, 22.7-23.0, 25.0-25.5, 26.0-26.2, and 27.4-27.6 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.

12. (Cancelled)

13. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I obtainable by a purification process comprising the step of recrystallizing a crude preparation of SAHA from an organic solvent or a mixture of an organic solvent and water, wherein the organic solvent is at least one of methanol, ethanol or isopropanol, the SAHA Form I is ~~The SAHA Form I according to claim 8,~~ further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.

14. (Cancelled)

15. (Cancelled)

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16. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to any one of claims 8, 11, 13, 147 to 149, 156 and 157 wherein said organic solvent is ~~an alcohol~~ ethanol.

17. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to any one of claims 168, 11, 13, 147 to 149, 156 and 157 wherein said ~~alcohol-organic solvent~~ is methanol, ~~ethanol or isopropanol~~.

18. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to any one of claims 8, 11, 13, 147 to 149, 156 and 157, wherein said purification process comprises the step of recrystallizing said crude SAHA from an organic solvent, wherein the organic solvent is at least one of methanol, ethanol or isopropanol.

19. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim 18, wherein said organic solvent is ~~an alcohol~~ methanol.

20. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim ~~19~~18, wherein said ~~alcohol-organic solvent~~ is ~~methanol, ethanol or isopropanol~~.

21. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to any one of claims 8, 11, 13, 147 to 149, 156 and 157, wherein said purification process comprises the step of recrystallizing said crude SAHA from a mixture of an organic solvent and water, wherein the organic solvent is at least one of methanol, ethanol or isopropanol.

22. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim 21, wherein said organic solvent is ~~an alcohol~~ ethanol.

23. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim ~~22~~21, wherein said ~~alcohol-organic solvent~~ is ~~methanol, ethanol or isopropanol~~.

24. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim ~~23~~21, wherein said mixture of organic solvent to water comprises about 1-99% methanol, ethanol or isopropanol and about 99-1% of water.

25. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim ~~24~~21, wherein said mixture comprises about 15-85% methanol, ethanol or isopropanol and about 1-15% water.

26. (Currently Amended) The ~~SAHA Form-I~~ active ingredient according to claim ~~24~~21, wherein said mixture comprises about 85% methanol, ethanol or isopropanol and about 15% water.

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27. (Currently Amended) The ~~SAHA Form I~~ active ingredient according to any one of claims 2, 3, 138 and 139 ~~1-5 and 8-26~~, in plate shaped form.
28. - 107. (Cancelled)
108. - 119. (Cancelled)
120. - 137. (Cancelled).
138. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I characterized by an X-ray diffraction pattern including characteristic peaks at about 9.4, 17.5, 19.4, 20.0, 24.0, and 28.0 degrees  $2\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about  $164.4 \pm 2.0$ , as measured by a Perkins Elmer DSC 6 Instrument.
139. (Currently Amended) An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I characterized by an X-ray diffraction pattern including characteristic peaks at about 9.4, 17.5, 19.4, 20.0, 24.0, and 28.0 degrees  $2\theta$ , and lacking peaks at about 13.4-14.0 and 22.7-23.0 degrees  $2\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source.
140. (Currently Amended) The ~~SAHA Form I~~ active ingredient according to claim 139, wherein the SAHA Form I is further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about  $164.4 \pm 2.0$ , as measured by a Perkins Elmer DSC 6 Instrument.
141. (Currently Amended) The ~~SAHA Form I~~ active ingredient of any one of claims ~~2-5, 12-15, 2, 3, 8, 11, 13,~~ 138 and 140, wherein the DSC measurement is performed by heating from 50 °C at 10 °C per minute to at least 30°C above the observed melting temperature.
142. (Currently Amended) The ~~SAHA Form I~~ active ingredient of claim 141, wherein the DSC measurement is performed with Perkin Elmer standard aluminum DSC sample pans and covers, with a nitrogen gas purge rate at about 20 ml/min.
143. (Cancelled).
144. (Cancelled).
145. (Cancelled).

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146. (Cancelled)
147. (Currently Amended) ~~The SAHA Form I of claim 8, further~~ An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I obtainable by a purification process comprising the step of recrystallizing a crude preparation of SAHA from an organic solvent or a mixture of an organic solvent and water, wherein the organic solvent is at least one of methanol, ethanol or isopropanol, the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at about 9.4, 17.5, 19.4, 20.0, 24.0, and 28.0 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.
148. (Currently Amended) ~~The SAHA Form I of claim 8, further~~ An active ingredient consisting essentially of suberoylanilide hydroxamic acid (SAHA) Form I obtainable by a purification process comprising the step of recrystallizing a crude preparation of SAHA from an organic solvent or a mixture of an organic solvent and water, wherein the organic solvent is at least one of methanol, ethanol or isopropanol, the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at about 9.4, 17.5, 19.4, 20.0, 24.0, and 28.0 degrees 2 $\theta$ , and lacking peaks at about 13.4-14.0 and 22.7-23.0 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source.
149. (Currently Amended) ~~The SAHA Form I~~ active ingredient according to claim 148, further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about 164.4 $\pm$ 2.0, as measured by a Perkins Elmer DSC 6 Instrument.
150. (Currently Amended) ~~The SAHA Form I~~ active ingredient of claim 147 or 149, wherein the DSC measurement is performed by heating from 50 °C at 10 °C per minute to at least 30 °C above the observed melting temperature.

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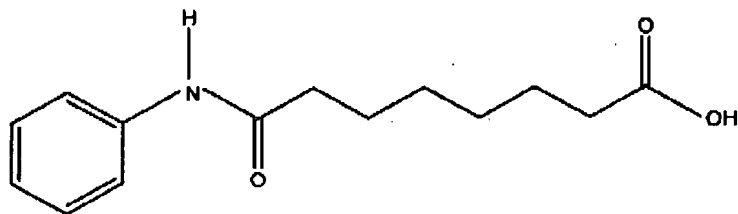
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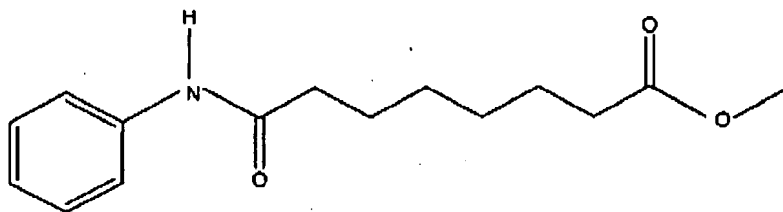
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Attorney Docket No. 24852-501 CIP

151. (Currently Amended) The ~~SAHA Form I~~ active ingredient of claim 150, wherein the DSC measurement is performed with Perkin Elmer standard aluminum DSC sample pans and covers, with a nitrogen gas purge rate at about 20 ml/min.
152. (Currently Amended) The ~~SAHA Form I~~ active ingredient according to claim 18, wherein said organic solvent is ethanol.
153. (Currently Amended) The ~~SAHA Form I~~ active ingredient according to claim 21, wherein said mixture of organic solvent to water comprises about 1-99% ethanol and about 99-1% of water.
154. (Currently Amended) The ~~SAHA Form I~~ active ingredient according to claim 21, wherein said mixture comprises about 15-85% ethanol and about 1-15% water.
155. (Currently Amended) The ~~SAHA Form I~~ active ingredient according to claim 21, wherein said mixture comprises about 85% ethanol and about 15% water.
156. (Currently Amended) The ~~SAHA Form I~~ active ingredient of claim ~~8148~~, wherein the crude preparation of SAHA is prepared by:
- a. reacting suberic acid with aniline to form suberanilic acid or a salt thereof having the structure:



- b. reacting suberanilic acid with methanol to form methyl suberanilate having the structure:



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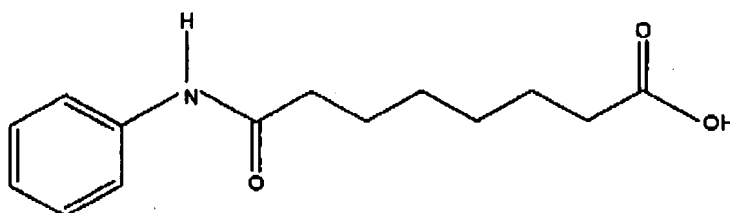
Attorney Docket No. 24852-501 CIP

- c. reacting the methyl suberanilate with hydroxylamine hydrochloride to form a crude suberoylanilide hydroxamic acid in a reaction mixture.
157. (Currently Amended) The ~~SAHA Form I~~ active ingredient of claim 156, further comprising the steps of:
- (1) adding sodium methoxide to the reaction mixture to obtain a clear solution; and
  - (2) adding glacial acetic acid to the clear solution to form a precipitate comprising crude suberoylanilide hydroxamic acid.
158. (Cancelled)
159. (Cancelled)
160. (Cancelled)
161. (Cancelled)
162. (Cancelled)
- 163 -172. (Cancelled)
173. (Currently Amended) An active ingredient consisting essentially of a A crystalline form of SAHA designated as Form I, wherein the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at about 9.4, 17.5, 19.4, 20.0, 24.0, and 28.0 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source, obtainable by a method comprising the step of recrystallizing a crude preparation of SAHA from a mixture of methanol and water.
174. (Currently Amended) The ~~crystalline form of SAHA~~ active ingredient according to claim 173, wherein said mixture of methanol and water is a mixture of about 2:1 of methanol/water.
175. (Currently Amended) An active ingredient consisting essentially of a A crystalline form of SAHA designated as Form I, wherein the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at 9.0, 9.4, 17.5, 19.4, 20.0, 24.0, 24.4, 24.8, 25.0, 28.0, 43.3 degrees 2 $\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; obtainable by a method comprising the steps of:

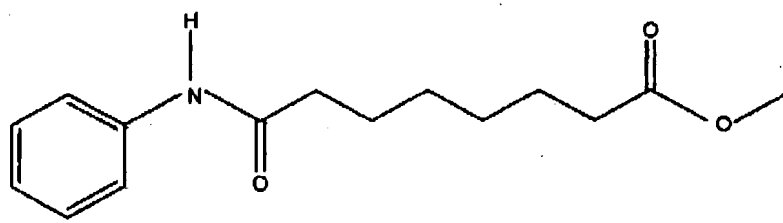
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Date of Transmissions: October 26, 2007

Attorney Docket No. 24852-301 CIP

- a. reacting suberic acid with aniline to form suberanic acid or a salt thereof having the structure:



- b. reacting suberanic acid with methanol to form methyl suberanilate having the structure:



- c. reacting the methyl suberanilate with hydroxylamine hydrochloride to form a crude suberoylanilide hydroxamic acid in a reaction mixture; and
- d. recrystallizing said crude preparation of SAHA from a mixture of methanol and water.
176. (Currently Amended) The ~~SAHA~~ active ingredient according to claim 175, wherein said mixture of methanol and water is a mixture of about 2:1 of methanol/water.
177. (Currently Amended) The ~~crystalline SAHA~~ active ingredient according to claim 175, wherein step (c) further comprises the steps of:
- (1) adding sodium methoxide to the reaction mixture to obtain a clear solution; and
  - (2) adding glacial acetic acid to the clear solution to form a precipitate comprising crude suberoylanilide hydroxamic acid.
- 178 -182. (Cancelled)



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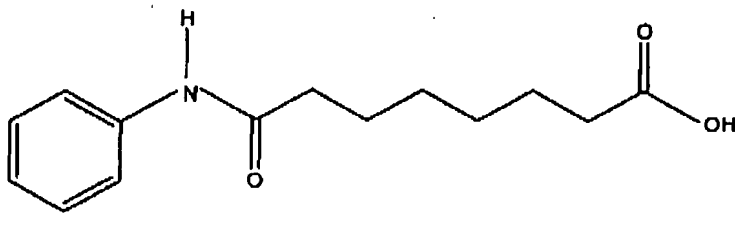
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183. (New) An active ingredient consisting essentially of a crystalline form of SAHA designated as Form I, wherein the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at about 9.4, 17.5, 19.4, 20.0, 24.0, and 28.0 degrees  $2\theta$ , and lacking peaks at about 13.4-14.0 and 22.7-23.0 degrees  $2\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; obtainable by a method comprising the step of recrystallizing a crude preparation of SAHA from a mixture of methanol and water.

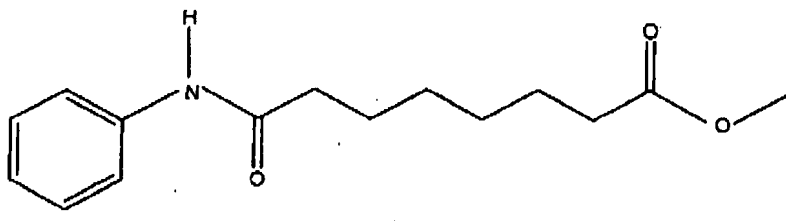
184. (New) The active ingredient according to claim 183, wherein said mixture of methanol and water is a mixture of about 2:1 of methanol/water.

185. (New) An active ingredient consisting essentially of a crystalline form of SAHA designated as Form I, wherein the SAHA Form I is characterized by an X-ray diffraction pattern including characteristic peaks at 9.0, 9.4, 17.5, 19.4, 20.0, 24.0, 24.4, 24.8, 25.0, 28.0, 43.3 degrees  $2\theta$ , wherein the X-ray diffraction is measured with a Copper X-ray source; and further characterized by a Differential Scanning Calorimetry (DSC) thermogram having a single maximum value at about  $164.4 \pm 2.0$ , as measured by a Perkins Elmer DSC 6 Instrument; obtainable by a method comprising the steps of:

- a. reacting suberic acid with aniline to form suberanilic acid or a salt thereof having the structure:



- b. reacting suberanilic acid with methanol to form methyl suberanilate having the structure:



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- c. reacting the methyl suberanilate with hydroxylamine hydrochloride to form a crude suberoylanilide hydroxamic acid in a reaction mixture; and
- d. recrystallizing said crude preparation of SAHA from a mixture of methanol and water.

186. (New) The active ingredient according to claim 185, wherein said mixture of methanol and water is a mixture of about 2:1 of methanol/water.

187. (New) The active ingredient according to claim 185, wherein step (c) further comprises the steps of:

- (1) adding sodium methoxide to the reaction mixture to obtain a clear solution; and
- (2) adding glacial acetic acid to the clear solution to form a precipitate comprising crude suberoylanilide hydroxamic acid.